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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/654,293 | 09/01/2000 | Leandro Christmann | AVI-005 | 5636 |

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AVIGENICS, INC.
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ATHENS, GA 30605

EXAMINER

TON, THAIAN N

| ART UNIT | PAPER NUMBER |
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1632

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/654,293

Applicant(s)

CHRISTMANN ET AL.

Examiner

Thaian N. Ton

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 34-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>3/01</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' Request for Continued Examination (RCE) filed 6/18/04 has been entered. Claims 1-33 have been cancelled. Claims 34-56 have been added and are under current examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-56 are rejected under 35 U.S.C. 112, first paragraph, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

The newly added claims 34-56 are directed to methods of enucleating a cell comprising visualizing internal structure of a cell utilizing a two-photon laser scanning microscope and ablating a nucleus, thereby enucleating a cell. The newly added claims constitute the introduction of new matter into the disclosure because they are not the specifically contemplated invention supported by the specification.

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The instant specification teaches that TPLSM [two-photon laser scanning microscopy] can be used in producing noninvasive, three-dimensional, real-time images of the optically dense oocyte [*e.g.* avian oocytes] and be used in enucleation [see specification pp. 13-14, bridging ¶] in the context of producing donor cells for nuclear transfer methods [see specification, p. 6, lines 11-20]. While the specification provides literal support for the newly added claims, they are not directed the subject matter that is found to be the invention contemplated by the instant specification because the only contemplated invention supported by the specification is methods of nuclear transfer in avians utilizing TPLSM to produce enucleated avian oocytes.

To the extent that the claimed methods are not described in the instant disclosure, claims 34-56 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In *re* Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those

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skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure" (emphasis added).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 34, as written, is indefinite. The claim recites "ablating a nucleus" in line 3 of the claim. It would be expected that the cell would only have one nucleus, it is suggested that the claim be written to state, "ablating the nucleus".

Claims 44-47 and 53-56 are confusing. The claims recite, for example, " ... wherein an oocyte comprises the cell." See claim 44. This is unclear because claim 34 does not recite any oocyte. Appropriate correction is requested.

Claim 42 is unclear because it recites that the nucleus is, "ablated mechanically". This is unclear if the mechanical ablation constitutes an additional

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step to the claim, or how it is further limiting to the steps presented in the independent claim. Appropriate correction is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 37-41 and 48-51 are rejected under 35 U.S.C. 102(b) as being anticipated by König *et al.* [Nature, 377:20-21 (September 5, 1995)].

The claims are directed to methods of enucleating a cell comprising visualizing the internal structure of a cell utilizing a two-photon laser scanning microscope and ablating a nucleus, thereby enucleating the cell.

König compare the cell damage on optically trapped motile human spermatozoa trapped by near-infrared microbeams with trapping effects at 760-800 nm compared to a continuous wave Ti:sapphire laser coupled to a fluorescence microscope. See p. 20, 1st column, 2nd ¶. The cells showed damage at 636 nm, see Figure 1 and p. 20, 2nd column. König state that the cloning efficiency of Chinese hamster ovary (CHO) cells was tested and that cells irradiated at 760 nm were unable to form clones. See p. 21, 1st column, 2nd full ¶. König conclude that

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continuous-wave near-infrared microbeams can cause membrane permeability, change cloning efficiency, and induce UVA-like stress (p. 21, col. 1-2, bridging ¶).

Note that the cell damage described by König is sufficient to anticipate the claims because the cells are unable to divide, which would constitute ablation of the nucleus and thus fulfill the limitation of ablation of the nucleus and the subsequent enucleation of the cell. König anticipate the claimed invention because they teach visualization of a cell utilizing a two-photon microscope within the range required by the claim [700-1000 nm] and that human spermatozoa and CHO cells incurred cell damage. Accordingly, because König teaches the steps required by the claims, they anticipate the claimed invention.

Claims 34-41 and 48-51 are rejected under 35 U.S.C. 102(b) as being anticipated by König *et al.* [Human Reprod., 11(10):2162-2164 (1996)].

König teach that near infrared laser radiation may induce cell damage. They teach that near infrared trapped sperm with exposure of less than 800 nm induces UVA-like biological effects, particularly oxidative stress, and particularly that sperm trapping at 760 nm caused cell paralysis and cell death at longer exposures. See Abstract. König teach that spermatozoa subjected to 760 nm traps caused reduced motility, paralysis and loss of viability. See Table 1 and p. 2163, col. 1-2, bridging ¶. König teach that optical traps at the short-wavelength part of near-infrared spectral region can cause cell damage and cell death. See p. 2164, 1st ¶.

Accordingly, König anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42-47 and 52-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell *et al.* [WO 97/07668, published 6 March 1997] when taken with König *et al.* *Nature*, 377:20-21 (September 5, 1995), and further in view of Squirrell *et al.* [Nat. Biotech., 17:763-767 (1999), Reference C29 of IDS filed 3/01].

Campbell teach teaching the reconstitution of an animal embryo by transfer of a diploid nucleus in an enucleated oocyte or to a fertilized one-celled zygote that has had both pronuclei removed [see p. 2, lines 7-16]. They teach that these methods of nuclear transfer can be used in all animals, including birds such as domestic fowl. See p. 5, lines 14-16. They teach that the recipient cells that can be used can be enucleated by any means, such as physical, actual removal of the nucleus, pro-nucleus, or metaphase plate (depending on the recipient cells) or functionally, for example by UV radiation or another enucleating influence. See p. 10, lines 12-16.

Campbell do not teach the specific enucleation of an oocyte by methods of two-photon laser scanning microscope. However, prior to the time of the claimed invention, Squirrell teach the use of two-photon laser microscopy at 1047 nm and 13 mW to image mammalian (hamster) embryos, and that by utilizing TPLSM, the embryos maintained developmental competence, as evidenced by the production of three near-term golden hamster fetuses and one live golden hamster pup. See p. 765, 2nd column, 1st ¶ and Figure 3. König compare the cell damage on optically trapped motile human spermatozoa trapped by near-infrared microbeams with trapping effects at 760-800 nm compared to a continuous wave Ti:sapphire laser coupled to a fluorescence microscope. See p. 20, 1st column, 2nd ¶. The cells showed damage at 636 nm, see Figure 1 and p. 20, 2nd column. König state that the cloning efficiency of Chinese hamster ovary (CHO) cells was tested and that cells irradiated

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at 760 nm were unable to form clones. See p. 21, 1st column, 2nd full ¶. König conclude that continuous-wave near-infrared microbeams can cause membrane permeability, change cloning efficiency, and induce UVA-like stress (p. 21, col. 1-2, bridging ¶) that results in the ablation of the nucleus. Thus, König provides a methods for the visualization and conditions that result in the nuclear ablation of a cell. Moreover, König provides the conditions necessary to practice the claimed method in embryonic cells.

In view of the combined teachings of Campbell, Squirrell and König, it would have been obvious for one of ordinary skill in the art to enucleate an oocyte by visualization and ablation of the nucleus utilizing TPLSM, with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to enucleate oocytes utilizing TPLSM because Campbell teaches enucleation of the oocytes by any means to produce oocytes for nuclear transfer, and Squirrel and König teach that TPLSM, can be used to both visualize and ablate the nucleus of a cell.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Amy Nelson, Acting SPE of Art Unit 1632, at (571) 272-0804. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

tnt

Thaian N. Ton
Patent Examiner
Group 1632

A handwritten signature in cursive script, appearing to read "Joe W. W. W.", written in dark ink.

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